PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : C12Q 1/68, G01N 33/574 — A1

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(22) International Filing Date: 21 January 2000 (21.01.00)

(30) Priority Data:
60/116,551 21 January 1999 (21.01.99) US

(71) Applicant *(for all designated States except US)*: BOARD OF REGENTS OF THE UNIVERSITY OF NEBRASKA [US/US]; Regents Hall, 3835 Holdrege Street, Lincoln, NE 68598 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: LIN, Ming–Fong [US/US]; 327 S. 92nd Street, Omaha, NE 68114 (US).

(74) Agents: KLANN, Ellen, M. et al.; Dann, Dorfman, Herrell and Skillman, Suite 720, 1601 Market Street, Philadelphia, PA 19103 (US).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: THERAPEUTIC AND DIAGNOSTIC APPLICATIONS OF PROSTATIC ACID PHOSPHATASE IN PROSTATE CANCER

(57) Abstract

Presented is a therapeutic method to treat prostate carcinomas in mammals comprising the administration of cellular PAcP protein. Also presented is a method to diagnose androgen–insensitive prostate carcinomas by determining the expression level of cellular PAcP in the prostate carcinomas, a decrease in expression being indicative of androgen–insensitivity. A promoter region that is specifically expressed in prostate tissue is presented, as is a xenograft animal model that mimics human prostate carcinomas in the expression of cellular PAcP.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
27 July 2000 (27.07.2000)

PCT

(10) International Publication Number
WO 00/43474 A3

(51) International Patent Classification[7]: C11D 1/22

(21) International Application Number: PCT/US99/29838

(22) International Filing Date:
15 December 1999 (15.12.1999)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/116,513 20 January 1999 (20.01.1999) US

(71) Applicant *(for all designated States except US)*: **THE PROCTER & GAMBLE COMPANY** [US/US]; One Procter & Gamble Plaza, Cincinnati, OH 45202 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **KOTT, Kevin, Lee** [US/US]; 2920 Bentbrook Drive, Cincinnati, OH 45251 (US). **SCHEIBEL, Jeffrey, John** [US/US]; 6651 Miami Trails Drive, Loveland, OH 45140 (US). **SEVERSON, Roland, George** [US/US]; 10184 Amberwood Court, Cincinnati, OH 45241 (US). **CRIPE, Thomas, Anthony** [US/US]; 599 Three Chimneys Lane, Loveland, OH 45140 (US). **BURCKETT-ST. LAURENT, James, C., T., R.** [GB/US]; 11477 Gideon Lane, Cincinnati, OH 45249 (US). **SCHEPER, William, Michael** [US/US]; 2393 Picnic Woods Drive, Lawrenceburg, IN 47025 (US). **KASTURI, Chandrika** [US/US]; 10044 Cliffwood Court, Cincinnati, OH 45241 (US).

(74) Agents: **REED, T., David** et al.; The Procter & Gamble Company, 5299 Spring Grove Avenue, Cincinnati, OH 45217-1087 (US).

(81) Designated States *(national)*: BR, CN, CZ, CZ (utility model), JP, MX, RU, US.

(84) Designated States *(regional)*: European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published:
— *with international search report*

(88) Date of publication of the international search report:
1 November 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 00/43474 A3

(54) Title: DISHWASHING COMPOSITIONS COMPRISING MODIFIED ALKYLBENZENE SULFONATES

(57) Abstract: The present application relates to hand dishwashing detergent compositions containing modified alkylbenzene sulfonate surfactants (MABS). These MABS comprise a mixture of specific branched and non-branched sulfonate compounds, which are further characterised by a 2/3-phenyl index of 160-275.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/29838

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C11D1/22

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C11D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 00 12451 A (PROCTER & GAMBLE) 9 March 2000 (2000-03-09) page 26, paragraph 3 page 54, paragraph 3 -page 58, paragraph 5 examples 4,7,8 ---	1-9, 13-19, 21-26, 30,31,34
P,X	WO 99 05244 A (PROCTER & GAMBLE) 4 February 1999 (1999-02-04) page 8, paragraph 6 -page 19, paragraph 2 example 13 claims 1-9 ---	1,2,5, 17,18, 21-32, 34-39 6-9, 14-16
	-/---	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 March 2000	19/04/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Bertran Nadal, J

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/29838

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	WO 99 07656 A (PROCTER & GAMBLE) 18 February 1999 (1999-02-18) page 19, paragraph 4 page 22, paragraph 4 -page 23, paragraph 1 page 34, paragraph 3 -page 45, paragraph 4 examples 1-8 claims 1-21	1-18, 21-26, 30,31, 34,39
A	EP 0 615 968 A (UOP INC) 21 September 1994 (1994-09-21) page 6, line 12 -page 7, line 39 claim 6	1-9,13, 14,16,39
A	US 4 301 316 A (YOUNG LEWIS B) 17 November 1981 (1981-11-17) cited in the application abstract column 3, line 21 -column 4, line 25 example 2 claims 1-5,7,10,11	1-15

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 99/29838

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 0012451	A	09-03-2000	NONE		
WO 9905244	A	04-02-1999	AU	8124998 A	16-02-1999
WO 9907656	A	18-02-1999	AU	8771998 A	01-03-1999
EP 0615968	A	21-09-1994	AU	658272 B	06-04-1995
			CA	2091855 A	18-09-1994
			JP	2055238 C	23-05-1996
			JP	6271485 A	27-09-1994
			JP	7084396 B	13-09-1995
			US	5196574 A	23-03-1993
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			AU	3529893 A	29-09-1994
			DE	69318393 D	10-06-1998
			DE	69318393 T	03-09-1998
			ES	2115015 T	16-06-1993
			DK	653179 T	09-02-1998
US 4301316	A	17-11-1981	CA	1149420 A	05-07-1983
			EP	0030084 A	10-06-1981

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 26 January 2001 (26.01.01)	
International application No. PCT/US00/01599	**Applicant's or agent's file reference** UNMC 63131PCT
International filing date (day/month/year) 21 January 2000 (21.01.00)	**Priority date** (day/month/year) 21 January 1999 (21.01.99)
Applicant LIN, Ming-Fong	

1. The designated Office is hereby notified of its election made:

   [X] in the demand filed with the International Preliminary Examining Authority on:

   18 August 2000 (18.08.00)

   [ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

   [ ] was not

   made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	*Authorized officer* Kiwa Mpay
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/01599

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :C12Q 1/68; G01N 33/574
US CL :435/6; 435/7.23

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6; 435/7.23

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, STN, MEDLINE, BIOSIS , CAPLUS, EMBASE, GENBANK
search terms: prostate, PACP, therapy, treatment, diagnosis, liposome

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,773,215 A (HANAUSEK-WALASZEK et al) 30 JUNE 1998(30.06.98), see entire document.	1-20, 22-25
Y	US 5,763,202 A (HOROSZEWICZ) 09 JUNE 1998(09.06.98), see entire document.	1-6
Y	SHARIEF et al. Nucleotide Sequence of Human Prostatic Acid Phosphatase ACPP Gene, Including seven Alu Repeats. Biochem. and Mol. Biol. International. June 1994. Vol. 33. No.3, see entire document.	1-20 and 22-25.
Y	OSTANIN. K. et al. Heterologous Expression of Human Prostatic Acid Phosphatase and Site-directed Mutagenesis of the Enzyme Active Site. The Journal of Biological Chemistry. 25 MARCH 1994. Vol. 269. No. 12, see entire document.	1-20 and 22-25

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 20 APRIL 2000	Date of mailing of the international search report 08 JUN 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer ARUN K. CHAKRABARTI Telephone No. (703) 308-1235

Form PCT/ISA/210 (second sheet)(July 1992) ★

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/01599

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	PORVARI. K. et al. Differential Androgen Regulation of Rat Prostatic Acid Phosphatase Transcripts. Biochemical and Biophysical Research Communications. 24 AUGUST 1995. Vol. 213. No. 3, pages 861-868, see entire document.	1-20 and 22-25
Y	US 5,763,415 A (SUKUMAR) 09 JUNE 1998(09.06.98), see entire document.	1-13
X,P	US 5,935,818 A (ISRAELI et al) 10 August 1999(10.08.99), see entire document, especially column 1, lines 20-60.	1-20 and 22-25
Y,P	US 5,882,864 A (AN et al) 16 March 1999(16.03.99), see entire document.	1-20, 22-25

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/01599

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 21 and 26-31
because they relate to subject matter not required to be searched by this Authority, namely:

Claim 21 contains SEQ ID NOs: 3 and 4 but no CRF and sequence listing was provided by the applicant. Claims 26-31 were not searchable because there are two claims with the same number 26.

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: KATHLEEN D. RIGUAT
DANN, DORFMAN, HERRELL AND SKILLMAN
1601 MARKET STREET
SUITE 720
PHILADELPHIA, PA 19103

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing *(day/month/year)*	17 MAY 2001
Applicant's or agent's file reference: UNMC 63131	IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/US00/01599	21 JANUARY 2000	21 JANUARY 1999

Applicant
BOARD OF REGENTS OF THE UNIVERSITY OF NEBRASKA

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer ARUN CHAKRABARTI
Facsimile No. (703) 305-3230	Telephone No. (703) 308-1235

Form PCT/IPEA/416 (July 1992)★

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference UNMC 63131	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/01599	International filing date *(day/month/year)* 21 JANUARY 2000	Priority date *(day/month/year)* 21 JANUARY 1999
International Patent Classification (IPC) or national classification and IPC IPC(7): C12Q 1/68; G01N 33/574 and US Cl.: 435/6; 435/7.23		
Applicant BOARD OF REGENTS OF THE UNIVERSITY OF NEBRASKA		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 12 sheets.

   [✓] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I [X] Basis of the report
   - II [ ] Priority
   - III [X] Non-establishment of report with regard to novelty, inventive step or industrial applicability
   - IV [ ] Lack of unity of invention
   - V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI [ ] Certain documents cited
   - VII [ ] Certain defects in the international application
   - VIII [ ] Certain observations on the international application

Date of submission of the demand	Date of completion of this report
18 AUGUST 2000	10 APRIL 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer ARUN CHAKRABARTI Telephone No. (703) 308-1235

Form PCT/IPEA/409 (cover sheet) (July 1998)★

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/01599

I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed

☒ the description:
pages (See Attached) , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the claims:
pages (See Attached) , as originally filed
pages _____ , as amended (together with any statement) under Article 19
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the drawings:
pages (See Attached) , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the sequence listing part of the description:
pages (See Attached) , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

☒ the description, pages NONE

☒ the claims, Nos. NONE

☒ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/01599

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 21 and 26-31

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination *(specify)*.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _ are so unclear that no meaningful opinion could be formed *(specify)*.

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 21 and 26-31.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/01599

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	1-20, 22-25, 32, 34	YES
	Claims	NONE	NO
Inventive Step (IS)	Claims	33	YES
	Claims	1-20, 22-25, 32, 34	NO
Industrial Applicability (IA)	Claims	1-20, 22-25	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-20 and 22-25 lack an inventive step under PCT Article 33(3) as being obvious over Horoszewicz (U.S. Patent 5,763,202) in view of Ostanin et al. (The Journal of Biological Chemistry, 1994) further in view of Sukumar (U.S. Patent 5,763,415) further in view of Provari et al. (Biochemical and Biophysical Research Communications, 24 August, 1995).

Horoszewicz teaches a therapeutic method for treating a mammalian prostate carcinoma, comprising the step of administering a therapeutically effective amount of cellular protein to the carcinoma (Abstract and Example 5, section 5.8, Columns 10-12).
Horoszewicz teaches a therapeutic method wherein the cellular protein is from human (Example 6).
Horoszewicz teaches a therapeutic method wherein the cellular protein is coupled to a monoclonal antibody (Example 5, Section 5.8.3).
Horoszewicz teaches a therapeutic method wherein the monoclonal antibody is immunologically specific to a human prostate cancer cell (Example 5, Section 5.8.3).
Horoszewicz teaches a diagnostic method wherein the cellular protein is quantified by an antibody immunologically specific to the cellular protein.(Example 5, Section 5.8.1).
Horoszewicz does not teach the therapeutic method wherein the cellular protein is PAcP and it is expressed by administering a nucleic acid comprised of the coding sequence of cellular PAcP.
Ostanin et al. teach the therapeutic method wherein the cellular protein is PAcP and it is expressed by administering a nucleic acid comprised of the coding sequence of cellular PAcP (Abstract Experimental Procedure Section).
Horoszewicz does not teach the therapeutic method wherein the expression vector is operably linked to the coding sequence of cellular protein.
Ostanin et al. teach the therapeutic method wherein the expression vector is operably linked to the coding sequence of cellular protein (Figure 1).
(Continued on Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Horoszewicz in view of Ostanin et al. further in view of Sukumar do not teach the method to diagnose androgen-insensitive prostate carcinomas.
Porvari et al. teach the method to diagnose androgen-insensitive prostate carcinomas. (Abstract).
Horoszewicz in view of Ostanin et al. further in view of Sukumar do not teach the method of quantifying the concentration of cellular PAcP protein in the prostate carcinoma.
Porvari et al. teach the method of quantifying the concentration of cellular PAcP protein in the prostate carcinoma by measuring mRNA by Northern blotting and determining acid phosphatase activity.(Figures 1 and 2).
Horoszewicz in view of Ostanin et al. further in view of Sukumar do not teach the promoter region useful for prostate specific expression, comprising the regulatory region of a PAcP gene having Genbank accession No: X47961.
Porvari et al. teach the promoter region useful for prostate specific expression, comprising the regulatory region of a PAcP gene having Genbank accession No: X47961. (Abstract and Page 861, Footnote).
Horoszewicz in view of Ostanin et al. further in view of Sukumar do not teach a xenograft model for studying human prostate cancers, comprising an athymic mammal hosting at least one transgenic human prostate carcinoma cell derived from LNCaP.
Porvari et al. teach a xenograft model for studying human prostate cancers, comprising an athymic mammal hosting at least one transgenic human prostate carcinoma cell derived from LNCaP. (Abstract, Introduction and Discussion Section).
It would have been obvious for an ordinary practitioner to substitute and combine the androgen action animal model tissue of Porvari et al. in the method of detecting prostate carcinoma of Horoszewicz in view of Ostanin et al. further in view of Sukumar, since Porvari et al. state, "One advantage of using an animal model is the availability of normal prostate, whereas studies of human prostate have to be carried out using mainly hyperplastic or cancerous tissue (Page 861, Introduction Section, lines 1-3)". An ordinary artisan skilled in the art would have been motivated to substitute and combine the androgen action animal model tissue of Porvari et al. in the method of detecting prostate carcinoma of Horoszewicz in view of Ostanin et al. further in view of Sukumar in order to achieve the express advantages, as noted by Porvari et al. of a method which provides advantage of using an animal model with the availability of normal prostate, whereas studies of human prostate have to be carried out using mainly hyperplastic or cancerous tissue.

Moreover, it would have been obvious to an ordinary practitioner to combine all the reagents and methods to use them as taught by Horoszewicz (U.S. Patent 5,763,202) in view of Ostanin et al. (The Journal of Biological Chemistry, 1994), further in view of Sukumar (U.S. Patent 5,763,415) further in view of Provari et al. (Biochemical and Biophysical Research Communications, 24 August, 1995) in the form of a kit, since the kit format saves money and resources for everyone by dramatically reducing waste and the other service provided in a kit is quality control.

Claims 1-20, 22-25, 32 and 34 lack an inventive step under PCT Article 33(3) as being obvious over Horoszewicz (U.S. Patent 5,763,202) in view of Ostanin et al. (The Journal of Biological Chemistry, 1994) further in view of Sukumar (U.S. Patent 5,763,415) further in view of Provari et al. (Biochemical and Biophysical Research Communications, 24 August, 1995)further in view of Barker et al. (U.S. Patent 5,814,630) (September 29, 1998).
Horoszewicz in view of Ostanin et al. further in view of Sukumar further in view of Provari et al. teach the method of claims 1-20, 22-25 as described above. Horoszewicz in view of Ostanin et al. further in view of Sukumar further in view of Provari et al. do not teach the method for diagnosing prostate tumor progression by a marker comprising elevated phosphotyorosyl ErbB-2 levels as compared to levels present in normal prostate tissue controls. Barker et al. teach the method for diagnosing prostate tumor progression by a marker comprising elevated phosphotyorosyl ErbB levels as compared to levels present in normal prostate tissue controls. (Column 1, line 34 to column 2, line 17).
It would have been obvious for an ordinary practitioner to substitute and combine the teaching of diagnosing prostate tumor progression by a marker comprising elevated phosphotyorosyl ErbB levels of Barker et al in the method of detecting prostate carcinoma of Horoszewicz in view of Ostanin et al. further in view of Sukumar, since Barker et al. state, "It is also known that EGF type tyrosine kinase activity is rarely detected in normal cells whereas it is more frequently detectable in malignant cells (Column 2, lines 8-11)". An ordinary artisan skilled in the art would have been motivated to substitute and combine the teaching of diagnosing prostate tumor progression by a marker comprising elevated phosphotyorosyl ErbB levels of Barker et al in the method of detecting prostate carcinoma of Horoszewicz in view of Ostanin et al. further in view of Sukumar in order to achieve the express advantages, as noted by Barker et al. of a method which provides advantage of pathological markers e.g., EGF type tyrosine kinase activity that is rarely detected in normal cells whereas it is more frequently detectable in malignant cells.

Claim 33 meets the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest to detect ErbB-2 levels by Western blotting.

---------- NEW CITATIONS ----------
US 5,814,630 A (BARKER et al) 29 SEPTEMBER 1998, see entire document.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
page(s) 1-72, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
Page 77, filed with the letter of 19 March 2001

This report has been drawn on the basis of the claims,
page(s) 73-77, as originally filed.
page(s) NONE, as amended under Article 19.
page(s) NONE, filed with the demand.
and additional amendments:
Page 77, filed with the letter of 19 March 2001.

This report has been drawn on the basis of the drawings,
page(s) 1-19, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the sequence listing part of the description:
page(s) NONE, as originally filed.
pages(s) NONE, filed with the demand.
and additional amendments:
NONE

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
Horoszewicz does not teach the therapeutic method wherein the coding sequence of cellular PAcP protein encodes Genbank Accession No: M34840.
Ostanin et al. teach the therapeutic method wherein the coding sequence of cellular PAcP protein encodes Genbank Accession No: M34840 (Page 8971, column 1, footnote).
It would have been obvious for an ordinary practitioner to substitute and combine the human prostatic acid phosphatase with Genbank accession No; M34840 of Ostanin et al. in the method of detecting prostate carcinoma of Horoszewicz, as Ostanin et al. states, "Because of its clinical importance as a prostate tumor marker, human prostatic acid phosphatase is the most extensively studied of the high molecular weight acid phosphatases. (Page 8971, column 2, first sentence of second paragraph)". An ordinary artisan skilled in the art would have been motivated to substitute and combine the human prostatic acid phosphatase with Genbank accession No; M34840 of Ostanin et al. in the method of detecting prostate carcinoma of Horoszewicz in order to achieve the express advantages, as noted by Ostanin et al of a method which provides a clinically important prostate tumor marker, human prostatic acid phosphatase which is the most extensively studied of the high molecular weight acid phosphatases.

Horoszewicz in view of Ostanin et al. do not teach a therapeutic method wherein the cellular protein is in a liposome.
Sukumar teaches a therapeutic method wherein the cellular protein is in a lipofectin type lipophilic drug-containing liposome (Column 8, lines 1-12).
Horoszewicz in view of Ostanin et al. do not teach a therapeutic method wherein the nucleic acid administered comprises the coding sequence of cellular protein operatively linked to a herpes simplex virus or cytomegalovirus.
Sukumar teaches a therapeutic method wherein the nucleic acid administered comprises the coding sequence of cellular protein promoter is operatively linked to a herpes simplex virus or cytomegalovirus promoter. (Column 3, lines 36-41 and Examples 1 and 2).
It would have been obvious for an ordinary practitioner to substitute and combine the therapeutic method containing liposome and viral vectors of Sukumar in the method of detecting prostate carcinoma of Horoszewicz in view of Ostanin et al. since Sukumar states, "Suicide and apoptosis genes can be administered by way of a viral vector, such as adenoviral or retroviral vector (Column 6, lines 66-67)". An ordinary artisan skilled in the art would have been motivated to substitute and combine the therapeutic method containing liposome and viral vectors of Sukumar in the method of detecting prostate carcinoma of Horoszewicz in view of Ostanin et al. in order to achieve the express advantages, as noted by Sukumar of a method which provides administration of suicide and apoptosis genes by way of a viral vector.

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PATENT COOPERATION TREATY

PCT

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

From the INTERNATIONAL BUREAU

To:
KLANN, Ellen, M.
Dann, Dorfman, Herrell and Skillman
Suite 720
1601 Market Street
Philadelphia, PA 19103
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 27 July 2000 (27.07.00)	
Applicant's or agent's file reference UNMC 63131PCT	**IMPORTANT NOTICE**

International application No.	**International filing date** (day/month/year)	**Priority date** (day/month/year)
PCT/US00/01599	21 January 2000 (21.01.00)	21 January 1999 (21.01.99)

Applicant
BOARD OF REGENTS OF THE UNIVERSITY OF NEBRASKA et al

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
   AU,JP,KP,KR,US

   In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:
   AE,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CN,CR,CU,CZ,DE,DK,DM,EA,EE,EP,ES,FI,GB,GD,
   GE,GH,GM,HR,HU,ID,IL,IN,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD,MG,MK,MN,MW,MX,NO,
   NZ,OA,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,TZ,UA,UG,UZ,VN,YU,ZA,ZW
   The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on
   27 July 2000 (27.07.00) under No. WO 00/43548

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, **a demand for international preliminary examination** must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the **national phase**, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

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